

### REMARKS

Reconsideration and withdrawal of the rejections set forth in the Office action dated June 30, 2003 are respectfully requested. Applicants petition the Commissioner for a 1-month extension of time. A separate petition accompanies this response.

#### I. Interview Summary in accord with MPEP § 713.04

Applicants thank Examiner Chen for the courtesy of a telephone interview.

1. Claims 1 and 2 were discussed.

2. The specific prior art discussed was Huiying *et al.* (*Virologica Sinica*, 13:3:213 (1998)) and U.S. Patent No. 6,207,439.

3. The general thrust of the principal arguments are described in section II below with regard to the 35 U.S.C. §103 rejection.

#### II. Rejections under 35 U.S.C. §103

Claims 1-3, 5, 7, 9, 10, 13, and 15-18 were rejected under 35 U.S.C. §103 as allegedly obvious over Huiying *et al.* (*Virologica Sinica*, 13:3:213 (1998)) in view of Liao *et al.* (U.S. Patent No. 6,207,439).

This rejection is respectfully traversed for the following reasons.

##### A. The Invention

The present invention relates to an inactivated virus particle, as a reinforced immunogen, prepared from a culture of cells infected with virus belonging to a group of Japanese encephalitis viruses. The inactivated virus particle is prepared by a process comprising a step of inactivation followed by a step of purification solely by physical means. The inactivated virus particle when prepared by this process achieves a neutralizing antibody titer of the anti-serum obtained by immunization with the virus particles is about twice to about 10 times the neutralizing antibody titer of the anti-serum obtained by immunization with inactivated virus particles prepared from virus cultured in mouse brain.

Virus particles prepared by the process described, where (i) the step of inactivation precedes the step of purification and (ii) purification is solely by physical means, have an unaltered surface that preserves the correct steric conformation for presentation of the antigen to antibodies, leading to the high neutralizing antibody titer.

#### B. The Cited Art

HUIYING ET AL. relates to a method for large scale purification of Japanese Encephalitis (JE) vaccine in vero cells by (1) concentrating by ultrafiltration; (2) precipitating with protamine sulfate; and then (3) purifying by zonal centrifugation at non-continuous sucrose gradients. Huiying *et al.* make no mention of inactivating the vaccine.

LIAU ET AL. disclose a process for large-scale purification of a live Japanese encephalitis virus from JEV-infected mouse brains and cell cultures. The virus from cell cultures is purified by the steps of microfiltration, ultrafiltration, or gel filtration and then inactivated with an inactivating agent such as formalin or binary ethyleneimide (see Table 4, Col. 9).

#### C. Analysis

According to the MPEP §2143.03 "all claim limitations must be taught or suggested by the prior art. All words in a claim must be considered in judging the patentability of that claim against the prior art."

As noted above, the present invention relates to inactivated viral particles prepared by a process of (i) inactivation followed by (ii) purification solely by physical means.

Huiying *et al.* teaches purification of a vaccine by ultrafiltration and sulfuric acid protamine precipitation (page 4, lines 9-11). Nowhere does Huiying *et al.* make any mention of how or when the vaccine is inactivated.

Liau *et al.* teaches purification of live virus from cell culture sources (Col. 6, lines 7-9) by filtration. The live virus is then inactivated with an inactivating agent (Col. 6, lines 55-58). Thus, Liau *et al.* teach a purification step followed by an inactivation step.

Thus, the combination of Huiying *et al.* and Liau *et al.* can at most be relied upon for a teaching of purification by physical means followed by a step of inactivation. Hence, nowhere does either reference, taken alone or in combination, show or suggest inactivated viral particles prepared by a process of (i) inactivation followed by (ii) purification solely by physical means.

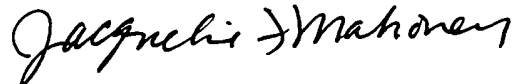
Accordingly, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. §103.

### **Conclusion**

In view of the foregoing, Applicants submit that the claims pending in the application are in condition for allowance. A Notice of Allowance is therefore respectfully requested.

If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 838-4410.

Respectfully submitted,



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